MARMITE

(YEAST EXTRACT)

IN MEDICINE AND DIETETICS

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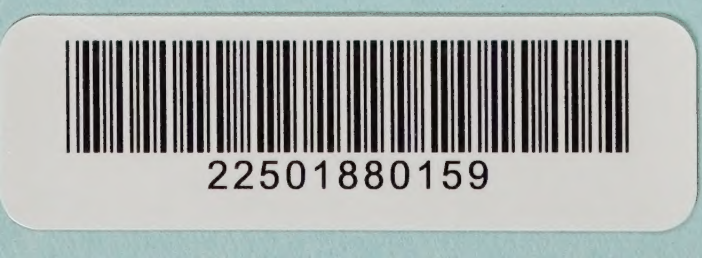

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DOSAGE TABLE

Indication	*Daily Dose*
Vitamin B Deficiency . . .	½ to 2 ounces
Infants	½ to 2 drachms
Œdema	3 drachms
Post-Operative Anæmia . . .	3 drachms
Tropical Macrocytic Anæmia . .	½ to 1 ounce
Anæmia of Cœliac Disease . .	3 drachms
Anæmia of Sprue	3 drachms
Pernicious Anæmia . . .	1½ to 4 ounces

The above table is given as a rough indication of the quantities of Marmite generally used in various conditions. It should be noted that a teaspoonful of Marmite is considerably more than 1 drachm—a point which has not been taken into consideration by all authors when writing case reports. In compiling this dosage table from such reports it has not always been possible to ascertain whether the Marmite was weighed or measured from a spoon. The appropriate dose for each case is best found by trial.

MARMITE

as source of

THE VITAMIN B COMPLEX

Nutrition and Health

The relation of nutrition to health has aroused widespread interest during the last few years. Among the authoritative reports issued on the subject those published by the League of Nations Committee and the Ministry of Health's Advisory Committee have attracted considerable notice.

These reports emphasise the special need for the adequate provision in the diet of protective foods, including particularly those of high mineral and vitamin content. It is stated (Advisory Committee 1937) that "*various mineral elements and vitamins play roles as essential in the economy of the body as those played by the proteins, fats and carbohydrates.*"

The detrimental effect as well as the prevalence of continued subsistence on foods lacking in the B vitamins is stressed by a number of clinicians and research workers.

Physicians have now recognised the importance of vitamin-containing foodstuffs in preventive and curative medicine ; they are prescribing Marmite increasingly in private practice and in hospitals, schools, welfare centres and clinics.

Marmite is an autolysed yeast extract ; it is one of the richest sources of the vitamin B complex (Medical Research Council Report 1932) and possesses valuable anti-anæmic properties.

The Vitamin B Complex

A few years ago only two vitamins of the B group were recognised. These were known as B_1, the anti-neuritic or anti-beri-beri factor, and B_2, the pellagra-preventive factor. Up to the present time at least six components have been differentiated, of which B_1, B_2, B_6 and the pellagra-preventive factor (P.P.) demand special attention.

Vitamin B_1, or aneurin, is the anti-beri-beri factor. Its action has been shown to be connected with carbohydrate metabolism (Peters 1936).

The original vitamin B_2 has proved to be a complex substance and the factor now designated B_2, or lactoflavin, is only one part of the B_2 complex. Lactoflavin is deemed important in cell oxidation but does not appear to prevent pellagra. Vitamin B_6 is also a portion of the B_2 complex, and "rat-pellagra" is thought by some workers to be associated with deficiency of this fraction. For the prevention of human pellagra yet another part of the B_2 complex is said to be required (Harris 1937), but little is known so far about this P.P. factor.

Vitamin Potency

Marmite contains all the known vitamins of the B complex, and its use in the treatment of diseases attributed to deficiency of these factors is well established.

In order to be able to express the B_1 potency of samples of Marmite in terms of the International Unit, several batches have been tested by a recognised authority using different samples of Marmite for each experiment.

Marmite is not standardised, but these estimations have shown the samples under investigation to contain 840 International Units of vitamin B_1 per ounce, or 30 International Units per gramme. The figures quoted above have been obtained by testing different samples of fresh material. Pigeons have been used as experimental animals and the technique has been that described by Coward, Burn, Ling and Morgan (1933).

In view of the known tendency of some vitamin preparations to lose in potency on storage, samples of Marmite taken from one particular batch have been examined at various intervals of time. These preliminary experiments indicate that the B_1 potency diminishes to a certain extent during the first 15 months. Thereafter no appreciable decrease has been observed when testing the same material after further periods of 6, 12 and 18 months. For most purposes this diminution in the B_1 content of Marmite may be of little importance, but the research worker who is seeking precise information upon some technical problem should take it into consideration.

No International Standards exist as yet for the other members of the vitamin B complex, and therefore no attempt has been made to estimate the content of these factors in Marmite.

Beri-Beri

Beri-beri is held to originate from a dietary deficiency of vitamin B_1, and the disease is curable by Marmite therapy. In Malaya, Java, India, Burma, China, Egypt, and other territories where beri-beri is prevalent, Marmite is prescribed systematically with beneficial results.

Platt and Lu (1936), recording their findings in cases of beri-beri in China, state : " *The patient had approximately 750 international units of vitamin B_1, mainly as Marmite. The œdema, cyanosis, and distressing dyspnœa and the sensation of epigastric oppression gradually subsided during the first 5–6 days · · · He was discharged at the end of one month apparently quite well.*"

Similar success obtained with Marmite therapy in cases of beri-beri is reported from Egypt, by Day (1936), who observes : " *Marmite was begun and within a week the œdema, ascites and enlargement of the liver had disappeared.*"

Gastro-Intestinal Disturbances

Many common disturbances of the alimentary system may be ascribed to avitaminosis B. Among others, McCarrison

(1936a) stresses the fundamental relation of vitamin B deficiency to gastro-intestinal dysfunction. Both the B_1 and B_2 fractions of the complex appear to be required for the functional efficiency of the tract, shortage of B_1 being associated with impairment of secretory and motor functions, while lack of the B_2 fraction is said to lead to degenerative and inflammatory conditions.

Describing the prevalence and consequences of mild degrees of vitamin deprivation, McCarrison (1936b) states : "*So, too, with vitamin B: poor appetite, some digestive disturbance, nervousness, feeble action of the heart, lack of vigour and fatigue may be evidences of its inadequate supply, where no signs of beri-beri exist.*" He emphasises the point that "*it is the lesser degrees of vitamin-deficiency, and the less obvious manifestations of such deficiency that are of importance in Western countries.*"

Many research workers and clinicians share the view that administration of the vitamin B complex is indicated for the prevention and treatment of gastro-intestinal disturbances. Marmite, being a palatable product, rich in all the known B vitamins, is particularly useful, and is widely prescribed for this purpose. It is frequently recommended for constipated patients, probably owing to its stimulating effect upon the gastro-intestinal tract.

Nervous Disorders

It is acknowledged that an adequate supply of the vitamin B complex is essential for the health of the nervous system ; that the polyneuritis of beri-beri is connected with deficiency of the B_1 factor, and that it responds to Marmite therapy. This form of treatment is now prescribed in many types of peripheral neuritis.

The frequent association of polyneuritis with gastric and intestinal symptoms is well known. In this connection the polyneuritis resulting from chronic alcoholism has recently been studied by various investigators. Since the lesions resemble those found in beri-beri, Strauss (1935) suggests that "*alcoholic polyneuritis may be regarded as similar to the*

polyneuritis of beri-beri and treated accordingly." He employs Marmite* treatment with success in this condition.

The vitamin B deficiency hypothesis is supported by Jolliffe, Colbert and Joffe (1936), who state further "*that polyneuritis in the alcohol addict is due to vitamin B deficiency.*" They suggest "*that the alcohol addict, to prevent a possible polyneuritis, should consume a full mixed diet supplemented by . . . vitamin B.*" They suggest that the quantity of vitamin required "*for each* 100 *calories of alcohol* (*about* 1 *ounce of whiskey*) . . . *can be conveniently obtained in about* 1 *gm. of Vegex.**"

It is interesting to note that the cardiovascular changes of alcoholic polyneuritis, like those of beri-beri, are also benefited by the exhibition of vitamin B_1 (Weiss and Wilkins 1936).

Skin Diseases

A number of skin complaints are amenable to Marmite treatment, which has proved especially efficacious in furunculosis and in skin conditions associated with constipation and defective diet.

Favourable reports have been published (Brown 1935) on the use of Marmite in leprosy, a disease that is endemic where dietaries are unsatisfactory and avitaminosis common. Brown has given regular supplements of Marmite to patients in a leper colony in Nigeria and the following notes from his case reports are interesting : "*Case* 59. *Complained of indigestion, irritation in the skin, and œdema. These disappeared with Marmite, and he was very emphatic about the improvement. . . Case* 10 . . . *The improvement was almost dramatic. Cod Liver Oil and Thyroid Extract had failed. Patient's comments endorsed the obvious improvement.*"

Experimental evidence indicates that susceptibility to leprosy infection may be increased by vitamin B deficiency, and analogies between beri-beri, pellagra and leprosy have been suggested.

* Marmite is known as Vegex in the U.S.A.

The value of Marmite in pellagrous skin lesions is mentioned below. In certain anæmias similar lesions have been found which " *responded as dramatically as the blood picture to the administration of Marmite* " (Vaughan and Hunter 1932).

Pellagra

The cause of pellagra is still doubtful, but it seems that the disease can be both prevented and cured by administration of the vitamin B_2 complex in the form of Marmite.

Recently Moore (1937) has commented on " *the dramatic effect of Marmite on the skin lesions* " of pellagrous conditions. After describing the prevalence of pellagrous symptoms among school children in Nigeria, he remarks that " *the disease is curable with Marmite . . .* " thus confirming his earlier observations on the subject. Moore reports that " *over* 200 *selected patients were treated for a period up to* 10 *months with yeast or Marmite alone—the majority with Marmite owing to its more stable properties. All skin conditions cleared up rapidly, and the visual response was entirely in keeping with results formerly obtained.*" In these cases retrobulbar neuritis and partial optic atrophy accompanied the pellagrous skin lesions.

Similar conditions, and equally successful results obtained with Marmite, have been recorded by Landor and Pallister in Malaya (1935), where the disease occurs with relative frequency in prisons and other institutions. The chief symptoms are skin eruptions, sore tongue and mouth,with loss of sensation, and retrobulbar neuritis in the later stages. Referring to the work of Landor and Pallister in a comprehensive survey, Stannus (1936) reports that " 50 *early cases were ' cured ' after* 15 *gm. Marmite daily for* 1 *month*, 20 *relapsed within a month of ceasing to take it !* "

Confirmatory evidence of the value of Marmite in pellagrous manifestations comes from West Africa (Dodds 1937), Egypt (1934), and India (Mody 1935). Gupta (1935), in publishing details of the recovery of a pellagra patient, remarks that " *the most important item in her treatment was*

the supply of vitamin B_2 ; she was given Marmite one teaspoonful thrice daily and improved steadily."

Œdema

There is sufficient clinical evidence to warrant the belief that treatment with vitamin B_1 is of value in cases of œdema. This is in accordance with the findings of Wills and Stewart (1935), who consider that the œdema sometimes associated with tropical macrocytic anæmia is related to deficiency of vitamin B_1.

Reduction of œdema following Marmite therapy has been noted by various research workers, including Wills (1931) and Vaughan (1932). Carmalt-Jones (1932) has directed special attention to the use of Marmite in œdematous conditions.

Prevention of Infection

The administration of Marmite appears to stimulate resistance to infection, and is therefore advocated in influenza epidemics and when other infectious diseases are prevalent.

The value of Marmite in this respect may be connected with the fact that the vitamin B complex "*contributes so markedly to the prevention of microbic invasion of the body.*" (McCarrison 1936b). It is now generally agreed that "*deficiency of the vitamin-B complex may be related to increased susceptibility to certain kinds of infection*" (Cowell 1937).

Restricted Diets

In limiting the selection of foods available by recommending a restricted diet it is important to guard against vitamin deficiency, and particular care is necessary to avoid a shortage of the vitamin B complex. It is largely for this reason that Marmite is ordered for inclusion in most invalid diets, and is listed on the diet sheets of many hospitals. It not only compensates for lack of vitamin B but at the same time provides an agreeable flavouring and stimulates the appetite. Its special value in anorexia is widely appreciated.

For diabetics and for those on a reducing diet Marmite is particularly indicated. It is a desirable constituent of a ketogenic diet, but may also be given with advantage when fat is prohibited. It has a special use in cœliac disease as it helps to combat the associated anæmia. T. P. Williams (1936) recommends the addition of Marmite to the diet of patients with colitis. He says : " *Medicinal treatment is not always required provided that we see that the vitamin requirements are satisfied, especially for the ' B ' complex.*"

In discussing the possible connection between colitis and deficiency of the vitamin B complex, Hare (1935) urges the addition of a liberal supply of vitamin B to the diet as a routine measure, and suggests the use of Marmite for this purpose. The administration of Marmite to colitis patients is also advocated by Graham (1935) and by Patterson (1936).

Many other conditions occur in which dietary restriction is essential and in which Marmite is of considerable value. It is useful, for example, in certain of the diets ordered for gastric and duodenal ulcer patients. Outlining the dietetic treatment of gastro-duodenal hæmorrhage, Witts (1937) states : " *Marmite is given at least once a day for the vitamin B complex.*" Wilkinson (1936) states that in cases of nutritional hypochromic anæmia " *the addition of one teaspoonful of Marmite daily . . . is of great value* " as there is a tendency to vitamin B_2 deficiency.

Pædiatrics

" *Vitamin requirements are admittedly greater during childhood than they are in later life . . .* " (McCance and Widdowson 1937). The health of the child is regarded as of such fundamental importance that the Mixed Committee on the Problem of Nutrition, appointed by the League of Nations, refer to it in their Interim Report (1936) as " *the kernel of the problem.*" In this report it is stated that " *pregnant women, nursing mothers, infants and young children must be considered from a nutritional standpoint as the most vulnerable portion of the population, in the sense that damage inflicted in childhood by bad food cannot be subsequently repaired.*"

Paterson maintains (1933) that "*the importance of vitamins in the diet of a child cannot be overestimated.*" In the opinion of Friend (1936) "*probably the B group is that most likely to be short in school diets . . .*" It is observed by Pritchard (1935) that "*the vitamin most commonly provided in insufficient quantity for toddlers is vitamin B.*" He recommends the systematic administration of Marmite to children whether healthy or sick, a procedure which is also advised by Parsons and Barling (1933).

The view is expressed in the Medical Research Council Report on vitamins (1932) that, as a safeguard, all children should be given "*Marmite for vitamin B complex—a small quantity daily.*" Children can often be tempted to eat Marmite sandwiches even when they refuse other food. It is therefore particularly useful for administration to debilitated children with anorexia. Marmite is also especially indicated in malnutrition, anæmia and wasting disease.

Pregnancy and Lactation

In discussing the nutritional needs in pregnancy at the annual meeting of the British Medical Association in 1937, special attention was directed to the spectacular fall in the mortality rate which has resulted from the supplementary feeding of expectant mothers in certain of the depressed areas.

It is reported that one speaker (Balfour 1937) "*commented on the success of the scheme initiated by the National Birthday Trust Fund for providing vitamin supplements. The mortality among* 7,000 *women taking the supplements had been* 1·69 *per* 1,000 *as compared with* 6·69 *per* 1,000 *among a comparable group of* 14,000 *women not taking supplements.*"

M'Gonigle (1937) says that "*those who have followed the interesting experiment carried out in South Wales under the direction of Lady (Rhys) Williams, in which the diet of expectant mothers has been very materially increased in regard to protein and the B group of vitamins among other supplements such as milk, must have been impressed with the results.*"

In December 1934, when medical experts recommended the free distribution of a few special foods to necessitous expectant mothers in the Rhondda Valley, Marmite was included in the short list of selected foodstuffs, and there is reason to think that the extra supply of the vitamin B complex thus provided may have played an important part in the prevention of disorders complicating pregnancy.

It is reported (J. E. Williams 1937b) that there have been only two maternal deaths in a continuous series of 2,328 unselected cases, extending over a period of 2½ years, among those mothers who have received Marmite. The drop in the puerperal death rate was so striking (from 11·29 in 1934 to 4·77 in 1935 per 1,000 total births) that application was made to the Commissioner for the Special Areas for a grant to provide for a similar experiment to be conducted in other depressed districts, and a grant was made in March 1936, to enable the scheme to be extended to parts of Durham and Monmouthshire (J. E. Williams 1936 ; 1937a).

Summarising the position, M'Gonigle (1937) states : " *If the results so far obtained during a relatively short time are continued it would appear as if the nutritional factor in maternal mortality is of the utmost importance and provides the key to the solution of a great social problem.*"

As an outcome of these and other investigations many doctors urge that Marmite should be added to the diet of all women as a routine measure during both pre-natal and post-natal periods.

According to McIlroy (1937) " *the diseases of pregnancy . . . should be classified as deficiency diseases.*" She remarks (1936) that on account of its vitamin content and its anti-anæmic properties, " *Marmite—a preparation of autolysed yeast—should be given in soups or as sandwiches with wholemeal bread and butter.*" Theobald (1935) suggests that all the toxæmias of pregnancy are due to dietetic deficiency, and (1937) that the vitamin B complex may be a main factor in their prevention. He recommends a well-balanced diet in which Marmite is included (1933).

MARMITE

as

ANTI-ANÆMIC AGENT

Great progress has been made recently in the study of hæmatology, and Marmite has been used by a number of workers who are investigating the nature of anti-anæmic principles.

In 1931 Wills made the discovery that Marmite possessed remarkable hæmopoietic properties and exerted a specific curative action in cases of tropical macrocytic anæmia. In 1932 it was noted by the Medical Research Council that "*this investigator observed dramatic improvement and cure when such cases were treated with a yeast extract (Marmite) rich in vitamins* B_1 *and* B_2." To-day there is general acceptance of the fact that this form of anæmia "*is invariably cured by Marmite*" (Vaughan 1936).

Tropical Macrocytic Anæmia

The original work on tropical macrocytic anæmia which led to the use of Marmite as a hæmopoietic agent was carried out in India, where this anæmia is a serious menace and has a particularly high incidence among pregnant women.

A study of the dietary habits of the patients suggested that malnutrition might be largely responsible for the disorder, and an attempt was made to improve their nutrition. The geographical distribution and the prevalence of tropical macrocytic anæmia also in China, Malaya and the West Coast of Africa support this view, which has since been corroborated by various investigators.

Marmite was included in the dietary scheme in India and it was found to cure the anæmia. Subsequently, Wills and Stewart (1935) succeeded in producing a similar form of anæmia in monkeys, by feeding them on a diet comparable with that in common use in the parts of Bombay where the incidence of tropical macrocytic anæmia is high. The monkeys were cured by Marmite therapy, the response being described as typical of that seen in cases of tropical macrocytic anæmia in humans.

Although this form of anæmia occurs with considerable frequency among pregnant women in tropical countries, it is also relatively common in non-pregnant women and in men, and is often associated with malaria and hookworm disease.

Confirmatory evidence has accumulated to show that Marmite provides a potent anti-anæmic substance. Wills (1933a) states : "*further trials have confirmed my previous findings as to the curative action of this preparation . . . in the majority of cases, even those with counts as low as one million, the response to Marmite in adequate doses is so rapid that the more expensive treatment is rarely necessary.*"

In 1934 the same investigator emphasised the importance of prevention and recommended that "*as a prophylactic measure, in areas where the condition is endemic, education and public health policy should encourage . . . the use of some autolysed yeast product such as Marmite.*" Recently (1937), she has reaffirmed that in this form of anæmia Marmite is curative by itself.

Napier (1936) has described a form of tropical macrocytic anæmia which differs in certain respects from that studied by Wills, but which also responds well to Marmite therapy. Whereas most of the patients treated by Wills were pregnant women, Napier's patients were all either men or non-pregnant women.

In the summary of his paper, Napier states : "*Among the cases of anæmia admitted to the Hospital for Tropical Diseases in Calcutta during the last year, there were* 11 *cases*

of macrocytic anæmia that responded to treatment with Marmite ; 4 of these patients were non-pregnant women and 7 were men." He is so convinced of the activity of Marmite that he has " *established a Marmite ' tradition ' in the hospital amongst patients and nurses.*"

Tropical Macrocytic Anæmia of Pregnancy

Several workers have published convincing corroborative accounts of the curative value of Marmite in tropical macrocytic anæmia of pregnancy. Reports have been issued from Bombay, Calcutta, Malaya and elsewhere. Thus Green-Armytage (1932), describing this anæmia, which is a grave social problem in India, records " *excellent results with Marmite given in 2 teaspoonful doses twice a day either in cold water or in soup. Marmite is very cheap and is uniformly more popular with patients than is liver, being of vegetable origin. In a consecutive series of 50 cases . . . the clinical and pathological state of the patient greatly benefited as a result of Marmite treatment.*"

In later reports (1934; 1935) Green–Armytage remarks that whereas the tropical macrocytic anæmias of pregnancy were hitherto " *often treated by liver or stomach preparations and there was no reticulocyte response, now . . . we can practically assure recovery by giving Marmite, ½ to ¾ oz. a day.*" He describes Marmite therapy as " *almost a specific method of treatment.*"

Cook (1935) comments upon the high mortality from tropical macrocytic anæmia among pregnant women in Uganda, where the disease has been confused with ankylostomiasis. He states that " *liver diet and Marmite seem the best remedies.*"

The specific use of Marmite in a similar form of anæmia occurring in British Guiana is described by Giglioli (1934 ; 1937). The anæmia is apparently not identical with that found in India, but it also affects pregnant women particularly, though not exclusively. It is suggested (Groen 1935 ; Groen and Snapper 1937 ; Fairley 1937) that the so-called " *tropical* " macrocytic anæmia is not confined to the tropics, but occurs relatively frequently also in Europe.

Anæmia of Sprue

The striking results observed when Marmite was used therapeutically in tropical macrocytic anæmia led to the consideration of its possible use in other types of macrocytic anæmia. Vaughan (1933) expresses the opinion that "*Marmite may safely be given indefinitely to those anæmias that respond satisfactorily.*" She recommends the trial of Marmite for two weeks wherever applicable in hyperchromic anæmias "*since it is far less expensive than liver or stomach.*" It has been suggested that, for all patients who are not desperately ill, Marmite should be tried before resorting to oral or parenteral liver therapy, as this yeast extract has proved curative alone in a large number of cases where the gastric secretion is not impaired.

It has been shown that in the anæmia associated with sprue "*many patients are greatly benefited by the oral administration of Marmite*" (Comrie 1937). Castle, Rhoads, Lawson and Payne (1935) record that in certain cases of sprue "*the effect of* 12 *Gm. of Vegex* was greater than the effect of liver extract derived from* 300 *Gm. of liver.*"

The inclusion of Marmite in the special diet sheets issued for patients with fatty diarrhœa and sprue is recommended by Graham (1935). Others who have prescribed Marmite in sprue with success are Rogers (1932) and Castle and Rhoads (1932).

Marmite therapy in sprue is a matter of routine in the Army Medical Service as well as in general hospitals and in private practice. Its use in sprue is noted in the Army publication "*Memoranda on Medical Diseases in Tropical and Subtropical Areas*, 1930" (H.M. Stationery Office), and also in "*Recent Progress in Medicine and Surgery*, 1919–1933."

Anæmia of Cœliac Disease

Vaughan and Hunter have studied the effect of Marmite on the macrocytic anæmia associated with cœliac disease. In 1932 they reported that "*the response of the anæmia to*

* Marmite is known as Vegex in the U.S.A.

Marmite was as dramatic as that obtained by the administration of liver extract in the treatment of Addisonian pernicious anæmia " and these findings were later substantiated (Bennett Hunter and Vaughan 1932 ; Vaughan 1936). Parsons and Smallwood (1935) note that " *rapid cure of some instances in adults suffering from cœliac disease has followed the administration of large doses of Marmite.*"

It has been observed that the macrocytic anæmia of cœliac disease may often be prevented if Marmite be given regularly, a custom which is commended by Parsons and Barling (1933), and also by Paterson and Forest Smith (1935).

Pernicious Anæmia

The use of Marmite in the treatment of pernicious anæmia has been investigated by several hæmatologists. A paper published in 1932 by Goodall stimulated interest in this subject. He reported as follows : " *Marmite in large doses is a satisfactory remedy for primary and relapse cases of pernicious anæmia of moderate severity . . . I have treated all my ' maintenance ' cases with Marmite. Without exception these have done well.*"

Corroborative evidence of its value in pernicious anæmia was published by Ungley (1932; 1933), who observed that " *in Addison's anæmia Marmite in doses of 4 oz. daily usually produces a satisfactory reticulocyte response.*" Further, that " *in addition to the effect of Marmite on blood regeneration and upon symptoms referable to anæmia, there occurred an increase in the sense of well-being, and a marked increase in appetite.*"

Wilkinson and Klein (1933) noted that several workers, including themselves, had " *obtained responses in cases of pernicious anæmia by the use of Marmite alone.*" Referring to pernicious anæmia, Vaughan (1936) states that " *certain patients respond to large doses of Marmite.*"

Marmite given alone or auxiliary to other treatment is welcomed by pernicious anæmia patients as it is palatable and inexpensive—two important considerations in prescribing a treatment which must be continued indefinitely. Marmite

therapy possesses obvious advantages over many forms of treatment ; it is recommended particularly for maintenance cases.

Ætiology of Macrocytic Anæmias

According to the theory postulated by Strauss and Castle (1932), normal hæmopoiesis is dependent upon the interaction of an intrinsic factor present in healthy human gastric juice, and an extrinsic factor supplied by certain food materials. Hyperchromic macrocytic anæmias are held to be due to a deficiency of this product of reaction—a deficiency which may be caused by lack of either the intrinsic or the extrinsic factor, or by inability to utilise the fully-formed product.

Research on the ætiology of the anæmias has centred round this hypothesis for some time, and it has been submitted that some macrocytic anæmias may be cured simply by supplying sufficient extrinsic factor, whereas in other anæmias, notably in Addisonian pernicious anæmia, there is also a deficiency of intrinsic factor, and cure is only possible if the complete hæmopoietic factor is supplied.

The Extrinsic Factor

In 1932 it was suggested that the extrinsic factor and vitamin B_2 were identical (Strauss and Castle). At this time, before the complex nature of vitamin B_2 was recognised, this supposition was contested. Wills (1934) conducted elaborate experiments which indicated that the hæmopoietic factor present in Marmite was not one of the known B vitamins. Similarly the experiments of Miller and Rhoads (1934) led to the conclusion that the anti-anæmic factor found in Marmite* is not vitamin B_2.

The fact that the extrinsic factor and vitamin B_2 are not identical was also shown by Lassen and Lassen (1934), and by Groen (1935) and others. In summarising the arguments in favour of the suggestion that the extrinsic factor and vitamin B_2 are separate entities, West (1935) states that Marmite* contains the extrinsic factor. Evidence of the

* Marmite is known as Vegex in the U.S.A.

dissimilarity between the Marmite hæmopoietic substance and the " *liver active principle* " has been presented by Ungley and James (1934).

Since the discovery that vitamin B_2 consists of more than one factor further enquiry has been made into the nature of anti-anæmic substances. Wills and others (1937) infer from recent work that the type of anæmia formerly attributed solely to lack of extrinsic factor, and consequent failure in production of active hæmopoietic principle, is also partly due to deficiency of a second hæmopoietic factor. This new factor has not yet been identified, but there is reason to believe that it may be related to the B_6 fraction of the vitamin B_2 complex.

Hæmopoietic Activity of Marmite

The hæmopoietic activity of Marmite was originally ascribed to its high content of vitamin B_2, and this vitamin was tentatively identified with Castle's extrinsic factor (Strauss and Castle 1932). This theory was disproved by Wills (1933b), who demonstrated that although Marmite is active curatively in cases of tropical macrocytic anæmia, other vitamin B preparations and yeast extracts are inactive. Wills states (1934) that " *dried yeast, watery yeast extracts, and preparations of the B vitamins from other sources (egg white and rice polishings) have been shown to be completely inactive.*"

From this work it was deduced that Marmite does not owe its hæmopoietic properties to its vitamin B content, but possibly to some protein breakdown product as yet unidentified. Parsons and Hickmans and their colleagues (1933), in studying nutritional anæmia, also found Marmite to be more effective than other yeast preparations.

The active principle was at this time held to be distinct from vitamin B_1, B_2 or B_4. Since the differentiation of vitamin B_2 into the fractions now known as lactoflavin and B_6, and since the reported existence of a new hæmopoietic factor (Wills and others 1937), the position becomes slightly altered although not yet clear.

It has been shown that lactoflavin is neither the hæmopoietic factor nor the extrinsic factor (Wills and others 1937; Groen 1935; Ashford and others 1936). It is apparent, however, that Marmite is a rich source of extrinsic factor and that it contains the hæmopoietic principle recently described by Wills, who thinks it likely that at least two hæmopoietic factors are present in Marmite.

The fact that Marmite alone has been observed to produce responses in some cases of Addisonian pernicious anæmia has lent support to the theory that it possesses an independent anti-anæmic factor. On the other hand, it has been suggested that the beneficial effect is due to the supply of extrinsic factor provided by Marmite, the assumption being made that, in the cases reported, the gastric secretion was only partially impaired and intrinsic factor not entirely lacking.

Whatever the ultimate explanation may be, the fact remains that the administration of Marmite in the treatment of certain types of anæmia is followed by dramatic results—in cases of tropical macrocytic anæmia Marmite therapy is regarded as a "*life-saving*" measure (Fairley 1935), and it has been described as "*the treatment of choice*" (Giglioli 1934).

MARMITE
in
TROPICAL MEDICINE

Avitaminosis B

Disease caused by dietetic inadequacy is known to be particularly common in tropical countries, and the prominent part played by deficiency of vitamin B_1 and the B_2 complex is engaging the attention of research workers and of Government authorities. The special applicability of Marmite—whether used as a medicine or as a food—in India and other tropical countries depends not only on its proved medicinal properties, but also on the fact that it is purely vegetable in origin and may therefore be taken freely by all those who, for religious or other reasons, insist upon a strictly vegetarian diet. Another point of practical importance is that it is economical in use and is not affected by climatic conditions.

Marmite is prescribed prophylactically and therapeutically in Malaya, India, Burma, China, Java and Egypt, to combat beri-beri, as mentioned on page 5. Reference to the use of Marmite in pellagra and allied conditions occurring in West Africa, Malaya, Egypt and India is made on page 8. In parts of East and Central Africa, and in many territories where poverty or dietary habits produce injurious effects upon the health of the people, Marmite is especially indicated and is being increasingly prescribed. It is considered useful for administration in leper colonies (page 7) and in communities suffering from epidemic malaria.

Tropical Macrocytic Anæmia

In cases of tropical macrocytic anæmia Marmite is regarded to be of specific value. The beneficial effects resulting from Marmite therapy in this form of anæmia, including the type associated with pregnancy, sprue, malaria and hookworm disease, are described on pages 13-16.

The number of papers published recently by experimental workers testifying to the efficacy of Marmite in tropical medicine affords ample proof of its value.

ADMINISTRATION

Marmite is exceptionally easy to administer on account of its palatability and the variety of appetising ways in which it may be served. Frequently it is given as a clear soup, prepared by stirring a small teaspoonful of the extract into a cupful of hot water. As a simple variation, a well-beaten egg may be added, or, when allowed, 1 or 2 teaspoonfuls of sherry. Marmite made with hot milk instead of water provides a particularly nourishing and pleasant beverage. It may, of course, be added to soups of all descriptions, thick and clear.

Iced Marmite is often appreciated, especially in hot climates and by invalids during warm weather. Marmite made into a paste with about three times the quantity of butter forms an appetising sandwich filling. This mixture may be spread on bread, toast, rusks or biscuits. As a culinary adjunct, Marmite may be incorporated in a variety of dishes—soups, sauces, stews, pies, gravies ; egg, cheese, fish, meat and savoury dishes. For invalids, and for vegetarians and those for whom a restricted diet is prescribed, Marmite is particularly useful.

For infants Marmite may be included in the ordinary feeds, and for older children it may be spread on rusks or served as broth. With children, as with adults, Marmite spread on bread and butter, or on buttered toast, is very popular.

Physicians who prescribe raw liver in the treatment of pernicious anæmia often advise that Marmite should be mixed with it, as this serves the double purpose of disguising, to a certain extent, the disagreeable flavour of the liver while enhancing its therapeutic effect. Patients report that this mixture is distinctly preferable to the raw liver.

The administration of sufficient active material is of the utmost importance in the treatment of pernicious anæmia; the failures recorded with liver therapy have been shown to be due usually to inadequate dosage, to inactive material or to septic foci. Similarly, in those anæmias which have been shown to respond to Marmite treatment, it is essential to eliminate septic conditions and to administer the appropriate quantity in order to achieve success.

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